REMARKS

As a result of the forgoing amendments, claims 10-27 are still pending. The preamble of claims 10, 12, 14, 15, 17, 19, 21, 23 and 25 have been amended to conform to US practice. Claims 11, 13, 16, 18, 20, 22, 24 and 26 have been amended to improve their grammar. Claims 12, 14, 15, 17, 19, 21, 23 and 25 have been amended to further define R^4 as an amino-protecting group as taught at page 2, line 8 of the specification. Claim 10 has been amended to define HX according to page 2, line 16 of the specification. Claim 25 has been amended to define R^1 according to the definition spanning pages 1 and 2 of the specification. Claim 17 has been amended to specify the absence of substantial amounts of other enantiomers, a limitation inherent from the process described on pages 7-8 for making compounds of formula (VIII). No new matter has been added as a result of these amendments. All of the limitations of the pending claims are clearly supported in the originally filed specification and/or claims. Accordingly, entry of the above amendments is proper.

The limitation added to claim 17, that the claimed compounds of formula (VIII) are substantially free of other enantiomers, is not new matter because it is inherent in the description of these compounds in the specification. As shown by the title of the application and throughout the specification, the claimed compounds are part of an asymmetric organic synthesis to produce a particular enantiomer of the end product. Accordingly, the intermediates of the synthesis scheme, such as the compounds of formula (VIII) claimed in claim 17, are particular enantiomers. That the particular enantiomer of a compound depicted by formula (VIII) is specifically synthesized and occurs in the absence of substantial amounts of other enantiomers is shown by the process taught by the specification for the production of the enantiomers of formula (VIII). The process disclosed on pages 7 and 8 of the specification uses a microorganism or an enzyme to specifically convert the substrate of formula (III) into the particular enantiomer depicted by formula (VIII). The use of the enzyme (either alone or in the microorganism) provides stereo-specificity to the reaction producing the compound of

formula (VIII), so that no substantial amounts of other enantiomers are formed. The absence of substantial amounts of other enantiomers of the compounds of formula (VIII) is inherent to the enzymatic reaction that produced the compounds of formula (VIII).

The allowance of claims 10, 11 and 27 and the Examiner's statement that the subject matter of claims 13, 16, 18, 20, 22 and 24 are allowable are appreciatively acknowledged.

§112 Rejections Should be Withdrawn

The above amendment to claim 25 clearly overcomes the rejection of that claim under 35 U.S.C. 112 for failing to contain a definition of R^1. This rejection should be withdrawn.

Reconsideration and withdrawal of the rejection of claims 12, 14, 15, 17, 19, 21, 23 and 25 under 35 U.S.C. 112, first and second paragraph, as requiring undue experimentation to practice or being indefinite for containing the term "protecting group", are respectfully requested. As noted above, the term "protecting group" has been amended in the instant claims to read "amino-protecting group". Applicants note that this amendment has no impact on whether the instant claims satisfy 35 U.S.C. 112. Although "amino-protecting group", as currently used in the claims, will be discussed in arguments below, all of the arguments would apply equally to a "protecting group", where the formula of the claims shows the "protecting group" to be bonded to a nitrogen atom.

The term "amino protecting group" is well-known in the art to which this invention belongs, organic synthesis. The claimed "amino protecting group" is a well known class of materials, all of whose members would be recognizable to one skilled in the art. As a demonstration of this, we searched the issued patent claims of the past 25 years on the USPTO website and found 588 patents with the term "amino protecting group" in the claims. Applicants also submit herewith a copy of the table of contents for

Chapter 7, "Protection for the Amino Group" from Protective Groups in Organic Synthesis by Theodora W. Green, published in 1981 by John Wiley & Sons, Inc. As shown in the table of contents for that particular chapter, "amino protecting groups" are well-known and exemplified by many members, all of which are within the skill of the art of organic synthesis. As shown by such text-book use, this term is well-known in the art and is in no way indefinite.

Terms that define a well-known class of materials, the members of which would be ascertainable to one skilled in the art, comply with 35 U.S.C. 112, first and second paragraph. In this manner, terms such as "water soluble hydrolyzable carbohydrate", *In re Skoll*, 187 USPQ 481 (CCPA 1975); "organic and inorganic acids", *In re Skoll*, supra; "inorganic salts", *In re Fuetterer*, 138 USPQ 217 (CCPA 1963); "polymerizable materials", *In re Bowen*, 181 USPQ 48 (CCPA 1974); and "organic radical", *In re Robins*, 166 USPQ 552 (CCPA 1970) have been held to comply with 35 U.S.C. 112, first and second paragraph.

The fact that the instant term "amino-protecting group" covers many different substituents is not a sufficient basis for a rejection under 35 U.S.C. 112. As stated by the CCPA in holding that the term "organic and inorganic acids" is not indefinite under 35 USC 112:

> We first consider the expression 'organic and inorganic acids', which is said to be indefinite and of uncertain scope. We cannot agree. Although there are undoubtably a large number of acids which come within the scope of 'organic and inorganic acids', the expression is not for that reason indefinite. We see no reason to believe that the public would be confused as to what subject matter is circumscribed by applicant's claim. *In re Skoll*, supra at 482.

The "amino-protecting group" term improperly rejected in this application is no less rigorously defined than the "organic and inorganic acids" upheld by the CCPA in *Skoll*. As noted above, applicants' "amino-protecting group" defines a well known class of substituents used in chemical synthesis, all of whose members would be recognizable to one skilled in the art.

The definition of the R^4 groups of the claims by their particular function, being amino-protecting groups, and not by particular chemical structures also fails to make the term or the claims indefinite under 35 U.S.C. 112. In reversing a 35 U.S.C. 112 rejection of a claim term to "an inorganic salt that is capable of holding a mixture of said carbohydrate and protein in colloidal suspension in water", the CCPA specifically approved use of such functional limitations:

> It is true that appellant's inorganic salt *is* defined in terms of "what it does" rather than "what it is." We note, however, that the Supreme Court, in a seldom quoted passage in the Wabash case, stated, 37 USPQ at 469:
>
> > A limited use of terms of effect or result, which accurately define the essential qualities of a product to one skilled in the art, may in some instances be permissible and even desirable ...
>
> Appellant in the instant case has made just such a use of terms of result to define an essential quality of his inorganic salts. (Emphasis in original) *In re Fuetterer*, supra at 222.

Accordingly, the instant rejection of claims under 35 U.S.C. 112 for containing the term "amino protecting group" is improper and should be withdrawn. "Amino-protecting group" defines a well-known and understood class of chemical groups, all of whose members would be recognizable to one skilled in the art; the instant term, claiming groups with the functional limitation that they are amino protecting, accurately defines the essential qualities of those particular groups to one of skill in the art; and the simple fact that the term is broad does not make it indefinite.

§102 Rejections Should be Withdrawn

The rejection of claim 23 under 35 U.S.C. 102(a) over either Lampe et al. or Adams et al. is improper and should be withdrawn. Applicants respectfully refer the Examiner to Formula X of claim 23, which clearly shows the hydroxyl and amino groups to be in a cis formation to each other (both groups are on the same side of the ring

structure). The compounds cited by the Examiner as anticipating claim 23 (compound 25 of Lampe et al. and compound 20 of Adams et al.) both clearly show a trans formation for the hydroxyl and amnio groups, meaning that each group is on a different side of the ring structure. The trans-configuration taught by Lampe et al. and Adams et al. does not encompass the cis compounds of claim 23.

The rejection of claim 25 under 35 U.S.C. 102(a) over Adams et al. is improper and should be withdrawn. Again, the instant claim specifies a cis arrangement between the hydroxyl group and the NHR^1 group, whereas the compound cited by the Examiner, compound 21 of Adams et al., is a trans arrangement. The trans-configuration taught by Adams et al. does not encompass the cis compounds of claim 25.

The rejection of claim 25 under 35 U.S.C. 102(a) over the disclosure of compounds B1-23 of Barbier et al. is improper and should be withdrawn. The exemplified compounds of Barbier et al. are all in the trans formation (3R, 4R). Again, the teaching of the trans formation does not anticipate the instantly claimed, structurally distinct, cis formation.

The rejection of claim 17 under 35 U.S.C. 102(a) over the disclosure of compounds 12 and/or 13 of Krogsgaard-Larsen et al. is improper and should be withdrawn. Compound 13 of Krogsgaard-Larsen et al. has a trans configuration between the hydroxyl and ester groups. Since compound 13 of Krogsgaard-Larsen et al. does not encompass the compounds of claim 17, which have a cis configuration between the hydroxyl and ester groups, compound 13 fails to anticipate claim 17.

Compound 12 of Krogsgaard-Larsen et al. is a racemic mixture of trans-hydroxy esters, including *both* an enantiomer according to instant formula (VIII) *and* the other possible trans-hydroxy ester, the structure shown for compound 12 in Scheme 2 of Krogsgaard-Larsen et al. Instant claim 17 has been amended above to require the absence of substantial amounts of enantiomers of the claimed compounds. Therefore,

claim 17 excludes the racemic mixture disclosed as compound 12 in Krogsgaard-Larsen et al. Furthermore, since Krogsgaard-Larsen et al. fails to teach or suggest any motivation or method for separating the racemic mixture into substantially pure isomers, Krogsgaard-Larsen et al. fails to enable or make obvious the instantly claimed enatiomerically pure compounds of formula (VIII).

§103 Rejection Should be Withdrawn

The rejection of claims 25 and 26 under 35 U.S.C. 103 over Barbier et al. is improper and should be withdrawn. Barbier et al. fails to place the compounds of instant claim 25 in the public domain because 1) the generic chemical formula III of Barbier et al. fails to disclose the instantly claimed compounds and 2) Barbier fails to provide an enabling disclosure of the instantly claimed compounds.

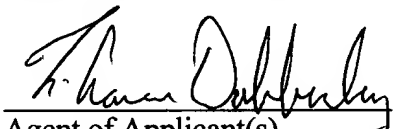
As the Examiner has correctly pointed out, a "generic chemical formula will anticipate a claimed species covered by the formula when the species can be 'at once envisioned' from the formula." Here, the instantly species of claim 25 cannot be "at once envisioned" from the generic chemical formula III of Barbier et al. Applicants respectfully submit that formula III of Barbier et al. encompasses millions of compounds. Note that A in the formula, is defined as in column 1, lines 20-30 can encompass any of at least 6 different ring structures with each and every ring atom being optionally substituted by lower-alkyl, lower-alkoxy and hydroxy groups, with some ring atoms having additional possible substitutents. Therefore, each position of each ring structure has at least 12 possible substituents, or $12^5 \cong 250{,}000$ possibilities per ring structure. Once all six possible ring structures are considered, there are at least 1.5 million possibilities. And once particular enantiomers of each of those compounds are taken into consideration, the number will be even greater. Applicants respectfully submit that the Examiner has yet to present any reason why the instantly claimed specific enantiomers can be "at once envisioned" from such a large group of possibilities. Accordingly, this rejection is improper and must fail.

The rejection of claims 25 and 26 under 35 U.S.C. 103 over Barbier et al. is also improper because Barbier fails to provide an enabling disclosure for the instantly claimed compounds (see MPEP 2121.02). The compounds of claims 25 and 26 are specific cis stereoisomers. These specific stereoisomers are necessary to obtain the object of the invention, the asymmetric synthesis of a biologically useful class of stereoisomers. Barbier et al. fails to teach or suggest to one of skill in the art how to make any cis isomers. Applicants respectfully note that *all* of the examples taught by Barbier (B1-23) are trans isomers. The disclosure of Barbier et al. leaves one of skill in the art with no direction as to how to make the cis compounds of claims 25 and 26. Particularly, there is no disclosure in Barbier et al. of how to make the particular cis isomer claimed, as opposed to the other possible cis isomer. Accordingly, this rejection is improper and must fail.

Attached hereto is a marked up version of the changes made to the specification and claims by their current amendment. The attached page is captioned **"Version with markings to show changes made."**

Applicants respectfully request that a timely Notice of Allowance be issued for this application.

Respectfully submitted,



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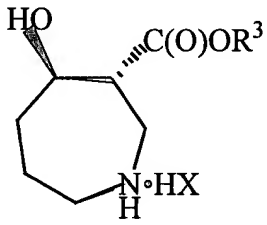
VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the claims:

10. (twice amended) A compound selected from the group consisting of compounds of the formula

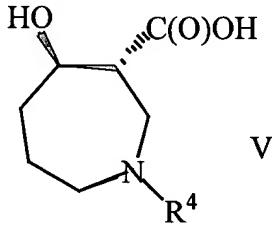


IV,

wherein R^3 is lower alkyl and HX is an acid.

11. (amended) The compound of claim 10, wherein the compound is ethyl (3R,4R)-4-hydroxy-azepan-carboxylate hydrochloride.

12. (twice amended) A compound selected from the group consisting of compounds of the formula

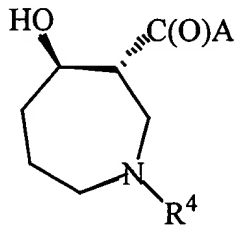


V

wherein R^4 is an amino-protecting group.

13. (amended) The compound of claim 12, wherein the compound is (3R,4R)-4-Hydroxy-azepan-1,3-dicarboxylic acid 1-tert.-butyl ester.

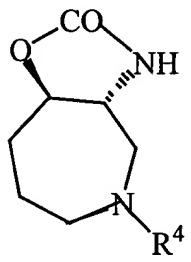
14. (twice amended) A compound selected from the group consisting of compounds of the formula



Va

wherein A is azido or amino and R^4 is an amino-protecting group.

15. (twice amended) A compound selected from the group consisting of compounds of the formula

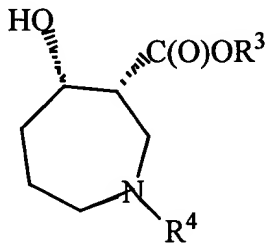


VI,

wherein R^4 is an amino-protecting group.

16. (amended) The compound of claim 15, wherein the compound is (3aR,8aR)-5-tert-Butoxycarbonyl-2-oxo-octahydro-oxazolo(4,b-c)azepine.

17. (twice amended) A compound selected from the group consisting of compounds of the formula

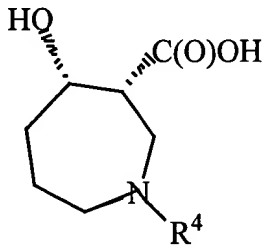


VIII,

wherein R^3 is lower alkyl and R^4 is an amino-protecting group,
in the absence of substantial amounts of other enantiomers of the compound.

18. (amended) The compound of claim 17, wherein the compound is ethyl (3R,4S)-1-(tert-butoxycarbonyl)-4-hydroxy-azepan-3-carboxylate.

19. (twice amended) A compound selected from the group consisting of compounds of the formula

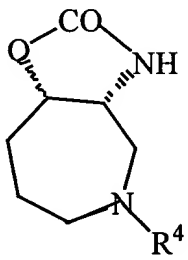


VIIIa,

wherein R^4 is an amino-protecting group.

20. (amended) The compound of claim 19, wherein the compound is (3R,4S)-4-Hydroxy-azepan-1,3-dicarboxylic acid 1-tert-butyl ester.

21. (twice amended) A compound selected from the group consisting of compounds of the formula

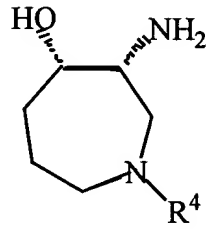


IX,

wherein R^4 is an amino-protecting group.

22. (amended) The compound of claim 21, wherein the compound is tert.Butyl (3aR,8aS)-2-oxo-octahydro-oxazolo(4,b-c)azepine-5-carboxylate.

23. (twice amended) A compound selected from the group consisting of compounds of the formula

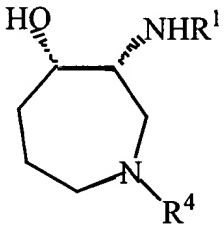


X,

wherein R^4 is an amino-protecting group.

24. (amended) The compound of claim 23, wherein the compound is tert-Butyl (3R,4S)-3-amino-4-hydroxy-azepan-1-carboxylate.

25. (twice amended) A compound selected from the group consisting of compounds of the formula



XI,

wherein R^1 is an acyl residue of an aromatic carboxylic acid and R^4 is an amino-protecting group.

26. (amended) The compound of claim 25, wherein the compound is tert-Butyl (3R,4S)-3-(4-tert-butoxy-benzoylamino)-4-hydroxy-azepan-1-carboxylate.